REMARKS

Claims 1-69 are pending in the application; claims 4-9, 11, 12, 14, 15, 17, 18, 20, 21, 23, 24, 26, 27 and 29-69 are withdrawn from consideration; claims 1-3, 10, 13, 16, 19, 22, 25 and 28 are rejected.

After entry of this amendment, claims 4-9, 11, 12, 14, 15, 17, 18, 20, 21, 23, 24, 26, 27, 29, 30, and 63-69 will be cancelled, and claims 1-3, 10, 13, 16, 19, 22, 25, 28 and 31-62 will be pending.

Claim 1 has been amended to include synthetic peptides within the scope of the claim. Support for the amendment may be found at page 9, line 6, of the specification.

Claim 1 has also been amended to recite that the alignment to the amino acid sequence of SEQ ID NO:1 is to the BH3 domain of the sequence. Support for the amendment may be found at page 43, lines 5-8, of the specification.

Claim 1 has been further amended to recite that the polypeptides encompassed within the scope of the claim have 95% sequence identity to SEQ ID NO:1. Support for this amendment may be found at page 46, lines 1-3.

No new matter has been added. Entry of this amendment is earnestly solicited.

I. Claim Cancellation

At page 2 of the Office Action, fifth paragraph, the Examiner states that a complete reply to the pending Office Action must include cancellation of the non-elected claims (namely, claims 4-9, 11, 12, 14, 15, 17, 18, 20, 21, 23, 24, 26, 27 and 29-69).

In response, Applicants note that under 35 U.S.C. §103(b)(i), a biotechnological process using or resulting in a composition of matter that is novel under §102 and non-obvious under

§103(a) shall be considered non-obvious if claims to the process and the composition of matter are contained in the same application. In other words, if claims to the mutant protein elected in response to the restriction requirement are allowed, Applicants may request allowance of claims to the methods of making and using the mutant protein and such claims should automatically be allowed.

Therefore, rather than canceling all of the non-elected claims, Applicants hereby assert that they wish to proceed under 35 U.S.C. §103(b)(i) and have claims to a method of making or using the mutant protein found allowable (claims 31-62) if the mutant protein is found allowable. Upon allowance of these claims, the non-elected subject matter recited in these claims will be cancelled as necessary.

As included herein, Applicants have also requested cancellation of the non-elected claims that do not recite a method of making or using the elected mutant protein (claims 4-9, 11, 12, 14, 15, 17, 18, 20, 21, 23, 24, 26, 27, 29, 30, and 63-69). Applicants reserve the right to file a divisional application on the cancelled claims.

In view of these comments, Applicants respectfully assert that the Examiner's requirement for cancellation of non-elected claims or other appropriate action has been met.

II. Rejection of Claims Under 35 U.S.C. §112

A. At page 2 of the Office Action, sixth paragraph, the rejection of claims 1-2, 10, 13, 16, 19, 22, 25 and 28[1] under 35 U.S.C. §112, first paragraph, as allegedly lacking enablement is maintained.

The Examiner maintains the rejection of the claims, first asserted in the Office Action dated December 19, 2001, as being non-enabled for an isolated polypeptide, or a fragment thereof, which does not have a serine at a position corresponding to position 118 of SEQ ID NO:1, wherein said position is identified by "alignment" of said polypeptide, or a fragment thereof, to SEQ ID NO:1.

The Examiner stated in the previous Office Action that the specification does not enable the skilled artisan to align sequences for comparison with SEQ ID NO: 1, to identify an amino acid at a position corresponding to serine 118 of SEQ ID NO: 1. Therefore, undue experimentation would be required to practice the claimed invention.

In response to Applicants' arguments asserted in the Amendment filed March 21, 2002, the Examiner admits that the specification discloses that an alignment may be performed using Lasergene software. However, the Examiner contends, the claims encompass any type of "alignment" of a polypeptide or a fragment thereof to SEQ ID NO:1, without any point of reference.

In response, Applicants include herewith an amendment to the claims to recite that the alignment is to the BH3 domain of SEQ ID NO:1. This domain is well known in the art, and as

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[1] Although claim 3 is not included in the list of rejected claims, in our opinion the Examiner mistakenly forgot to add it to the list.

shown in Figure 3A of the present application, the BH3 domains of different proteins can be readily aligned.

Further support for the ability of the skilled artisan to align and compare BH3 domains may be found in two articles published after the filing date of the present application. Datta et al. (2000) shows an alignment of the BH3 domain of BAD from different species in Figure 1A. Letai et al. (2002) provides an alignment of BH3 domains for a number of different proteins containing BH3 domains from a number of different species in Table 1. Copies of these papers are submitted herewith for the Examiner's convenience.

Thus, in view of the amendment to the specification, and the comments above, Applicants assert that the skilled artisan would be fully enabled to make and use the invention as recited in the pending claims. Therefore, Applicants respectfully request reconsideration and withdrawal of the rejection.

B. At page 3 of the Office Action, fifth paragraph, the rejection of claims 1-2, 10, 13, 16, 19, 22, 25 and 28[2] under 35 U.S.C. §112, first paragraph, as allegedly lacking enablement is maintained.

As in the previous Office Action, the Examiner states that the claims recite an isolated polypeptide, or fragment thereof, which contains a domain at least 75% homologous to a BH3 domain of wild-type BAD, and an isolated polypeptide or fragment thereof that is at least 75% homologous to SEQ ID NO:1 (human BAD).

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[2] Although claim 3 is not included in the list of rejected claims, in our opinion the Examiner mistakenly forgot to add it to the list.

The Examiner contends that the claims are not enabled because there is only support for such a BAD protein with a mutation at serine 118. The Examiner argues that the skilled artisan would not know where to make additional mutations to arrive at a BAD protein with the claimed activity. The Examiner states that no principle has been taught that correlates amino acid position with the ability to dephosphorylate and activate the BAD sequence. The Examiner asserts that screening for such proteins would be mere trial and error.

In response, Applicants have amended claim 1 to recite an isolated polypeptide, or fragment thereof, which has at least 95% homology with SEQ ID NO:1 (human BAD), that does not have a serine residue that corresponds to position 118 of SEQ ID NO:1, and that has cell death promoting activity.

Applicants assert that such an amended claim is clearly enabled by the specification. The group of polypeptides encompassed by the amended claim only includes those having at least 95% sequence homology with human BAD. This group is further limited by the requirement that a serine residue not be located at position 118, and that the polypeptides have cell death promoting activity. Applicants assert that this group of polypeptides is very small, and that the skilled artisan would readily understand which polypeptides would be included in the group, for example, those polypeptides identical to SEQ ID NO:1 having several point mutations that do not affect the activity of the polypeptide.

In view of the amendment to the claims, and the points discussed above, Applicants respectfully request reconsideration and withdrawal of the rejection.

III. Rejection of Claims Under 35 U.S.C. §102

At page 6 of the Office Action, second paragraph, the rejection of claims 1-2, 10, 13, 16, 19, 22, 25 and 28[3] under 35 U.S.C. §102(b) as allegedly being anticipated by U.S. Patent No. 5,965,703 is maintained.

The Examiner again states that SEQ ID NO: 3 of the '703 patent (mouse BAD) falls within the scope of the cited claims because it discloses a protein with a BH3 domain that has 75% homology to the BH3 domain of the present invention, with a threonine at a position corresponding to residue 118 of SEQ ID NO: 1, and with cell death promoting activity.

As to Applicants' arguments that the '703 patent does not have a disclosure that the protein encoded by SEQ ID NO: 3 (mouse BAD) has cell death promoting activity, the Examiner does not find such arguments persuasive. The Examiner states that the cell death promoting activity is an inherent property of BAD, including mouse BAD. The Examiner cites to U.S. Patent No. 5,622,852 for support of her position that mouse BAD can accelerate apoptotic cell death.

In response, Applicants assert that the amino acid sequence of the mouse BAD provided in the '703 patent, and shown in Figure 2 therein, is not correct. The amino acid recorded as "T" (threonine) at position 160 in the figure (the correct residue number would be 155 due to the empty positions at 77-81) should be recorded as "S" (serine).

In support of this position, Applicants point to Figure 1A of the Datta et al. publication discussed above. Therein, a portion of the amino acid sequence of mouse (*M. musculus*) is

[3] Although claim 3 is not included in the list of rejected claims, in our opinion the Examiner mistakenly forgot to add it to the list.

shown. As can be seen therein, a "S" appears at position 155. In addition, Table 1 of the Letai et al. reference discussed above also shows a "S" at the same position of the partial mouse BAD shown therein (third sequence from the top in the table, "mBADBH3").

Thus, as demonstrated above, Applicants assert that the skilled artisan working in this field understands that the amino acid sequence shown in Figure 2 of the '703 patent is not correct.

In view of the error in the '703 patent, Applicants assert that the mouse BAD disclosed therein would not anticipated the pending claims of the instant application. The mouse BAD of the '703 has a serine residue corresponding to position 118 of SEQ ID NO:1, and thus does not meet the requirement of claim 1 that the sequence "does not have a serine at a position corresponding to position 118 of SEQ ID NO:1."

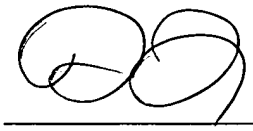
Accordingly, Applicants assert that the present invention is not anticipated by the '703 application, and respectfully request reconsideration and withdrawal of this rejection.

IV. Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,



SUGHRUE MION, PLLC
2100 Pennsylvania Avenue, N.W.
Washington, D.C. 20037-3213
Telephone: (202) 293-7060
Facsimile: (202) 293-7860

Drew Hissong
Registration No. 44,765

Date: October 18, 2002

APPENDIX

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

Claims 4-9, 11, 12, 14, 15, 17, 18, 20, 21, 23, 24, 26, 27, 29, 30, and 63-69 are canceled.

The claims are amended as follows:

1. (Amended) An isolated or synthetic polypeptide comprising an amino acid sequence of a mutant Bcl-X_L/Bcl-2 Associated Cell Death Regulator polypeptide (BAD), or fragment of said isolated or synthetic polypeptide comprising a less than full-length amino acid sequence of said mutant BAD, wherein:

a) said isolated or synthetic polypeptide, or said fragment, is ~~contains a domain~~ at least 95% ~~75%~~ homologous to SEQ ID NO:1~~a BH3 domain of a naturally-occurring or wild-type mammalian BAD~~;

b) said amino acid sequence of said isolated or synthetic polypeptide, or said amino acid sequence of said fragment, does not have a serine at a position corresponding to position 118 of SEQ ID NO:1, said position in said amino acid sequence of said isolated or synthetic polypeptide, or said position in said amino acid sequence of said fragment, being identified by alignment of said amino acid sequence of said isolated or synthetic polypeptide, or said amino acid sequence of said fragment, to the BH3 domain of SEQ ID NO:1; and

c) said isolated or synthetic polypeptide, or said fragment, has cell death promoting activity.